Rec'd PCT/PTO 04 MAY 2005 10533844

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number
WO 2004/041213 A2

(51) International Patent Classification[7]: A61K

(21) International Application Number:
PCT/US2003/035294

(22) International Filing Date:
4 November 2003 (04.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/424,031 4 November 2002 (04.11.2002) US

(71) Applicants *(for all designated States except US)*: **BIOARCTIC NEUROSCIENCE AB** [SE/SE]; Lagmansvagen 13, S-18163 Lidingo (SE). **ICOGEN CORPORATION** [US/US]; 454 North 34th Street, Seattle, WA 98103 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HAGEN, Frederick, S.** [US/US]; 1315 Lexington Way East, Seattle, WA 98112 (US). **LANNFELT, Lars** [SE/SE]; Vintertullstorget 28, S-11643 Stockholm (SE). **GELLERFORS, Par** [SE/SE]; Lagmansvagen 13, S-18163 Lidingo (SE).

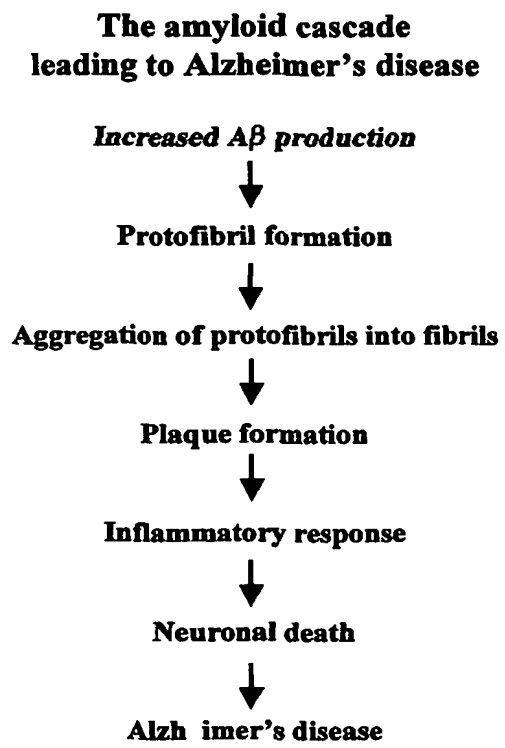
(74) Agents: **POOR, Brian, W.** et al.; TOWNSEND and TOWNSEND and CREW, LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHODS FOR THE IDENTIFICATION OF AGENTS THAT MODULATE THE STRUCTURE AND PROCESSING OF BETA-AMYLOID PRECURSOR PROTEIN



(57) Abstract: The present invention provides methods for the screening and identification of agents from a large library of molecular structures that can alter the cleavage of amyloid precursor protein (AP). Agents identified by the methods of the present invention that modify the cleavage of APP can be used in the treatment and prevention of Alzheimer's disease. The methods select for and identify effector agents that bind to APP causing a structural change in the structure of APP in such a way that the efficiency of the cleavage of a secretase is modulated. Further, the methods are carried out in an in vivo system that provides for physiological conditions similar or identical to conditions for APP processing. Agents can be selected for their ability to cause a decrease in the amount of ß-secretase or ?-secretase cleavage of APP, or for an increase in a-secretase cleavage of APP. The agents can be, particularly peptide agents, can be converted into a peptidominetic, an isosteric replacement compound, a D-amino acid analog, or non-peptidyl compound for treating Alzheimer's disease or any other amyloid related or prion related disease. The agents or derivatives thereof can be formulated for intravenous, parenteral, topical, sustained release, intranasal, or inhalation use.

WO 2004/041213 A2

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.